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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/578,194	05/24/2000	Marcelo Dornelas	026-1	5443

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EXAMINER
SCHMIDT, MARY M

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2635	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No	Applicant(s)
09/578,194	DORNELAS ET AL.
Examiner	**Art Unit**
Mary M. Schmidt	1635

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Status

1)☒ Responsive to communication(s) filed on 12/09/02.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4, 7-16 and 20-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4, 7-16 and 20-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).

4)☐ Interview Summary (PTO-413) Paper No(s).

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II, claims 1-24, and election of species of the dzeta ASK gene of Group II and the plant species *Arabidopsis* in Paper No. 9, filed 06/11/02, is acknowledged.

In the response filed 12/9/03, Applicant submitted a petition of the restriction requirement. The petition has been denied according to the "Petition Decision" letter, mailed 3/31/03. The requirement is still deemed proper and is therefore made FINAL. Please note the claims are considered on the merits only as they are drawn to the elected inventions: ASK dzeta antisense in *Arabidopsis*.

Claim Objections

2. Claims 1-4, 7-16 and 20-24 are objected to for the misspelling of the gene name ASKdzeta (ASKζ)-gene of group II, since the claims read "ASK dzet*h*a".

3. Claim 22 is objected to for the language, "the process *of* according to...".

4. Claim 23 is objected to for the language, "according to according to".

Improper Incorporation by Reference

5. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

6. The attempt to incorporate subject matter into this application by reference to Dornelas et al., Plant Mol. Biol. Vol. 39, 1999, pp. 137-147, (page 19, line 8, of the specification) is improper because the Dornelas et al. reference is relied upon to teach the claimed fragment of at least 150 bp to the 5'UTR and N-terminal region of the ASK dzeta gene, but incorporation of such essential material to the claimed invention is non properly incorporated from a non-patent publication according to MPEP 608.01(p)(A.). MPEP 608.01(p)(A) states that "An application as filed must be complete in itself in order to comply with 35 U.S.C. 112.... "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by

reference to... (2) non-patent publications...." The specification as filed does not teach the nucleic acid sequence by way of SEQ ID NO. of the ASK dzeta gene. Without the knowledge of this sequence in the specification, one of skill in the art would not be able to use the disclosed PCR primers to the ASK dzeta gene (page 19 of the specification) in order to make the claimed constructs for use in the claimed methods. See the 35 U.S.C. 112 rejections below.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4, 7-16 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 was amended to state a process for the production of a transgenic plant the seeds of which comprise an embryo exhibiting a modified cotyledons development, wherein at least one plant cell is transformed with at least one DNA cosuppression construct comprising a nucleic acid sequence derived from an ASKdzeta (ASK$_\zeta$)-gene of group II is a fragment of at least 150 base pairs corresponding to the 5' untranslated region and part of the N-terminal coding region

and regenerated to a plant whose embryos exhibit the modified development. Claim 2 was amended to state the process according to claim 1, wherein the nucleic acid sequence derived from an ASKdzeta (ASKζ)-gene of group II is a fragment of at least 300 base pairs corresponding to the 5' untranslated region and part of the N-terminal coding region. Claim 3 states that the modified development is characterized by the development of an increased number of cotyledons. Claim 4 was amended to state that the cosuppression construct is an antisense or sense construct or a construct comprising a transposable element wherein the DNA construct is capable of eliminating the expression of an endogenous ASKdzeta (ASKζ)-gene of group II. Claim 7 was amended to state the process according to claim 1, wherein the nucleic acid sequence derived from an ASK-gene of group II is a fragment of 150 to 350 bp, corresponding to the 5'-untranslated region and a part of the N-terminal coding region of ASKdzeta (ASKζ)-gene of group II. Claim 8 states the process according to claim 1, wherein the ASK-gene is in the form of a cDNA or genomic DNA. Claim 9 states the process according to claim 1, wherein the DNA construct comprises at least one regulatory element being operably linked to the nucleic acid sequence derived from the ASK-gene of group II and being capable of directing the expression of the nucleic acid sequence derived from the ASK-gene of group II. Claim 10 states the process according to claim 9, wherein the regulatory element is a promoter and or enhancer, in particular the 35 S CaMV-promoter. Claim 11 states the process according to claim 1, wherein the DNA construct comprises a transcription termination signal operably linked to the nucleic acid sequences derived from the ASK-gene of group II, in particular a poly A addition

site. Claim 12 states the process according to claim 1, wherein the DNA construct is cloned into a vector, in particular a plasmid or viral vector. Claim 13 is drawn to the process according to claim 1, wherein the plant cell is from a monocotyledonous or dicotyledonous plant. The process according to claim 13, wherein the monocotyledonous or dicotyledonous plant is Arabidopsis, brassica, cotton, potato, soya, sugar beet, sugar cane, an ornamental plant, rice, maize, barley or wheat. Claim 15 states the process according to claim 1, wherein the plant cell is transformed by transfer of the DNA construct by a method selected from the group selected from: transfer via a bacterium, transfer via virus to the cell, transfer via direct uptake of the DNA construct by microinjection of the DNA construct, transfer via direct uptake of the DNA construct by particle bombardment. Claim 16 is drawn to the process according to claim 1, wherein the transformed cell is regenerated into a differentiated plant. Claim 20 is drawn to a plant comprising at least one cell according to claim 13. Claim 21 is drawn to seeds and plant derived tissue comprising a genetically modified cell according to claim 20. Claim 22 is drawn to a plant produced according to the process according to claim 1. Claim 23 is drawn to seeds and plant derived tissue obtained from a plant produced by the process according to claim 1. Claim 24 is drawn to a transgenic Arabidopsis plant the seeds of which comprise an embryo exhibiting a modified cotyledons development, said plant comprising at least one plant cell transformed by a nucleic acid sequence derived form at least one ASKdzeta (ASKζ)-gene of group II wherein at least one embryo exhibits the modified development.

The specification as filed teaches that ASK stands for "Arabidopsis SHAGGY-related protein kinase" and is a multigene family including alpha, gamma, dzeta, etha and iota (page 2 of the specification). Note that in view of the restriction requirement, the instant claims are only examined in view of the ASK dzeta isoform. The specification teaches on page 19 that *Arabidopsis* plants were transformed using *Agrobacterium tumefaciens* containing antisense constructs including fragments from the 5' extremity of the ASK gene, obtained by PCR as taught in Dornelas et al. *Plant Molecular Biology* Vol. 39, pp. 137-147, 1999, but does not teach the nucleic acid sequences used by way of nucleic acid sequence.

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice.... reduction to drawings.... or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function

and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

To practice the steps of the claimed methods, and to visualize the claimed *Arabidopsis* seeds and plants having the claimed ASK dzeta antisense constructs, one of skill in the art would need to know the nucleic acid sequence of the ASK dzeta gene and or the actual nucleic acid sequence of the 150 bp or more fragment used as the antisense sequence corresponding the 5'-untranslated region and N-terminus coding region of the ASK dzeta gene. Absent this sequence information, one of skill in the art would not be able to readily envisage the claimed compositions in the methods steps and plant seed compositions. Although the specification provides PCR primers that provide a 300 base pair fragment used in the examples in the specification, one of skill in the art would not be in possession of the claimed fragment without the target gene sequence of the ASK dzeta gene from which to amplify via PCR the 300 bp fragment. Thus, the target gene ASK dzeta gene is considered "essential material" to the instantly claimed invention and is not properly incorporated by reference to the Dornelas et al. non-patent reference.

One of skill in the art would not have recognized that applicant was in possession of the claimed invention at the time the invention was made since the specification as filed has not adequately described a representative number of species of any ASK dzeta group II gene, nor fragments of at least 150 bases thereof that have the claimed functions of antisense inhibition of the ASK dzeta gene in *Arabidopsis*. Since the knowledge of the target ASK dzeta gene

sequence is essential material to the practice of the claimed invention and since the specification as filed did not teach the target ASK dzeta gene sequence nor the nucleic acid sequence of a representative number of fragments thereof, nor provides substantial incorporation by reference to the target gene in the prior art that is the ASK dzeta gene contemplated by the instantly claimed invention, one of skill in the art would not have recognized that application was in possession of the claimed invention as the time the invention was made. Nor is applicant in possession of "*an* ASK dzeta gene" since this implies that more than one ASK dzeta gene exists, the breath of which is not supported by either the specification as filed or the prior art.

9. Claims 1-4, 7-16 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for production of a transgenic *Arabidopis* embryos and seeds via administration of *Agrobacterium* containing ASK dzeta antisense constructs to the ASK dzeta gene for the resulting

development of increased number of cotyledons, does not reasonably provide enablement for production of transgenic *Arabidopsis* via antisense to any possible ASK dzeta gene for any modified development as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

See the description of the claims above.

The specification as filed teaches on pages 18-22 that administration of the ASK dzeta antisense to *Arabidopsis* leads to increased number of cotyledons. The specification does not teach any other phenotypic modification of embryos for administration of antisense to ASL dzeta. The specification further teaches that the modifications of claim 2, abortion of the embryo was observed only with administration of antisense to the ASKetha gene, and not via administration of antisense to the elected species, ASK dzeta.

At the time the invention was made, the prior art taught the isolation of ASK group II genes, but did not teach a conclusive role of these genes in plant development. Dornelas et al. (Plant Mol. Biol. 1999) taught hybridization assays to determine the expression levels of various ASK genes in plants at different developmental stages, but did not teach gene knock-out experiments to determine gene functions. (They only taught on page 146 that "[s]creening of T-DNA insertion lines and transgenic *Arabidopsis* plants containing anti-sense constructs for the ASK genes is taking way in our lab to access additional information concerning the role of the ASK genes on plant development.) Dornelas et al. (The plant journal, 21 (5), 419-429, 2000 (date of availability was 4.5.00)) taught that AtSK11 and 12 function in perianth and gynoecium development, but did not address ASK dzeta development. Piao et al. (Plant physiology, 4/99, vol. 119, pp1527-1534) taught the role of an ASK iota complementary gene in NaCl stress signal pathway, but does not address ASK dzeta development. Tichtinsky et al. (cited by Applicant on page 23 of the specification) taught the role of ASK beta and theta in developing pollen, but did not specifically address the role of ASK dzeta in development. Dornelas et al. (Gene 1998, cited

by Applicant on page 22 of the specification) taught a sequence structure and evolutionary comparison of the different ASK genes in *Arabidopsis*, but did not specifically teach the role of ASK dzeta in development.

As such, the prior art did not provide any guidance as to what the results would be achieved for administering antisense to an ASK dzeta for the modified development of *Arabidopsis* embryos. Only Applicants' invention has shown the ability to increase the number of cotyledons in *Arabidopsis* embryos upon administration of antisense to ASK dzeta. However, these results do not correlate with an expectation of success that design and administration of any other antisense to ASK dzeta gene would result in other "modified development" results in the transgenic plants claimed.

Furthermore, the claims are not enabled for making and using any 150 bp fragment of any possible ASK dzeta gene as claimed since the specification as filed did not provide an enabling disclosure at the time the invention was made for increasing the number of cotyledons in *Arabidopsis* by using any such antisense as broadly claimed. As pointed out above, the specification as filed did not provide the actual ASK dzeta gene sequence used to generate via PCR the 300 bp fragment used in the disclosed experiments. Thus, no real comparison can be made between the specification as filed and the Dornelas et al. references in the art since it is not explicitly taught that the instantly claimed ASK dzeta gene indeed has the same nucleic acid sequence as those taught by Dornelas et al. in the prior art. Absent this information, one of skill in the art would necessarily design *de novo* possible fragments of at least 150 bp which have the

claimed functions of increasing the number of cotyledons in an *Arabidopsis* plant. Furthermore, the high homology of the ASK gene family core region teaches that only certain regions of the ASK dzeta gene were available for the design of antisense specific to this ASK gene. As such, one of skill in the art would not have recognized that the use of antisense to other regions of the ASK gene for administration to *Arabidopsis* could be extrapolated to increase the number of cotyledons, the results taught in the instant specification, upon down-regulation of the ASK dzeta gene. Furthermore, Applicant has not provided guidance as to how to transform *Arabidopsis* in any other way, other than via *Agrobacterium*, so that other modified development results may be achieved other than increased number of cotyledons. In view of the teachings of the specification and of the prior art, and the lack of guidance for any other means for administration of antisense to ASK dzeta in *Arabidopsis* other that the methods exemplified in the specification, one of skill in the art would have had to practice an undue amount of experimentation to practice methods and make transgenic *Arabidopsis* plants and seeds with ASK dzeta antisense as claimed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Inquiries relating to the status of this application may also be directed to *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
March 30, 2003